

# Synthetic Organic Chemicals

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## Diazonium Compounds *Their Use in Organic Synthesis*

THE reactions of the diazonium compounds discovered by Griess in 1860 are very interesting, both commercially and from a scientific standpoint. The long list of azo dyestuffs manufactured in this country and abroad shows the importance of one of the basic diazo reactions known as "coupling." In this process, the diazonized amino compounds react with tertiary aromatic amines or phenols by joining directly to the carbon atom in the para position. The familiar indicator, methyl orange, is a simple azo dye prepared by coupling diazotized sulfanilic acid with dimethylaniline. Other dyes containing four or more azo groups prepared by successive diazotizing and coupling are not uncommon.

The diazonium salts, themselves, usually are formed by the action of sodium nitrite on primary amines in ice-cold acid solutions. They are soluble in water and most of them are unstable when dried, so the reaction mixture generally is used without attempting to isolate the salt. While the coupling property of diazonium compounds is of vast importance to the dye industry, it is seldom used in the laboratory in the preparation of organic chemicals. For obtaining many of the esters, phenols, halides, nitrites, ethers, other typical diazo reactions are of greater importance.

One of the most frequent laboratory

uses of the diazonium reaction is in the preparation of aromatic halogen derivatives. Although an aromatic nucleus can be halogenated directly with free chlorine or bromine, it is often difficult to control the position or number of halogen atoms entering the nucleus. Through the agency of the diazo reaction, almost any aromatic amine can be converted to the corresponding halogen derivative. The most common procedure, known as the Sandmeyer reaction, involves the use of cuprous chloride or bromide as the source of the halogen. To prepare p-chlorotoluene, the diazonium compound is first obtained by diazotizing p-toluidine. The solution is kept cool and treated with cold cuprous chloride which forms an addition compound. This intermediate product is readily decomposed by warming, and the p-chlorotoluene is separated from the reaction mixture by steam distillation. In a similar manner, m-bromotoluene, o- and p-bromonitrobenzenes, and o-bromobenzoic acid are prepared by the action of cuprous bromide, starting with the amino derivatives.

In the case of iodobenzenes, it is not necessary to have the copper salt present, since the addition of potassium iodide, with subsequent heating, is sufficient to convert the diazonium compound. This method is much to be pre-

ferred to direct iodination for preparing iodobenzoic acid and, in fact, nearly all of the aromatic iodo derivatives.

Since gaseous fluorine is not a commercial product, the preparation of aromatic fluoro-compounds through the diazonium reaction is one of the best methods. Benzene diazonium fluoride can be decomposed by heating, to give fluorobenzene, but it is difficult to keep the reaction running smoothly. However, if a mixture of boric and hydrofluoric acids is added to the benzene diazonium chloride solution, the solid diazonium boro-fluoride separates out. This can be dried, and the decomposition by heating controlled much more easily than is the case with the fluoride itself. Many of the fluorine derivatives recently added to our list were prepared by this general method.

The aryl diazonium salts are readily reduced to hydrazines with zinc and acetic acid, or by treating with sodium bisulfite and hydrolyzing the resulting salts. Reduction to the hydrocarbon may also take place when diazonium compounds are boiled with alcohols under proper conditions of temperature and pressure. This is not the usual procedure, however, as ethers are ordinarily formed by this reaction. Examples are anisole and phenetole, which can be readily prepared from the benzene diazonium compound by heating with methyl or ethyl alcohol. The same ethers would also be obtained by treating the aliphatic compounds, diazomethane or diazoethane, with phenol. Thio-ethers can be made in a similar manner by using mercaptans in place of alcohols. S-phenylcysteine is formed from benzene diazonium chloride and cysteine.

The principal reason for carrying out diazotizations at low temperatures is to prevent hydrolysis of the resulting compound. The hydrolysis may be useful, however, as in the formation of phenols from the corresponding amino com-

pounds. This reaction occurs with the evolution of nitrogen when aqueous solutions of the diazonium salts are warmed, except in the case of highly negative substituted amines, such as tribromoaniline.

Hydroxy acids also may be obtained by hydrolysis, diazo-acetic acid giving a quantitative yield of ethyl glycollate. The sulfur analogs would result if the hydrolysis were carried out with hydrogen sulfide, although the more common method of preparing thiocresols is to start with the xanthates. Potassium ethyl xanthate is added to a solution of the diazonium salt, and after heating to liberate the nitrogen, the resulting aryl xanthate is hydrolyzed. A recent adaptation of this method has led to the preparation of a number of aryl esters of dialkyl dithiocarbamic acids. Other esters may be prepared conveniently through the action of acetic acid or acetic anhydride on the diazonium group.

Aromatic nitriles can be synthesized by replacing the cuprous bromide in the Sandmeyer reaction, with cuprous cyanide. Contrary to the usual practice, in this case the diazonium salt is neutralized with sodium carbonate as soon as it is formed, in order to prevent the evolution of hydrogen cyanide and its attendant hazards.

Arsenic can be added to an aromatic nucleus by a similar reaction, as by adding a neutral solution of p-nitrobenzene diazonium chloride to a dilute solution of disodium ortho arsenic acid. A number of the arsenicals used in the treatment of trypanosome infections can be made in this way. Mercury also will replace the  $\cdot\text{NN}\cdot$  group.

As mentioned previously, the stability of the diazonium compounds varies greatly and, in most reactions, temperature is an important factor. In many instances, the salts are explosive so it is best whenever possible to work with them in solution or as moist solids.



## Liquids for Measuring Refractive Index

THE refractive index of a crystalline material usually is an important aid in identification. The immersion method for determining refractive index with the aid of a microscope is quite simple, and the technic is easily acquired. For most general laboratory work, the highly accurate determinations that may be made with a petrographic microscope are not required.

The immersion method consists in observing the appearance of the crystal when surrounded by a liquid whose refractive index is accurately known. A fragment of the specimen is arranged on a microscope slide and a drop of the liquid carefully manipulated until the crystal is completely surrounded. A cover glass may be used to prevent evaporation of the liquid.

Under the microscope, the particles are outlined by a shadowy line, the depth of which depends on the difference between the refractive index of the solid and that of the liquid. Theoretically, this line would disappear entirely if the two indices were equal, but usually some difference in color or dispersion of light enables the solid to be seen. The change produced in the illumination of the crystal when a part of the incoming light is shut off by the finger indicates whether a liquid of lower or higher refractive index should be tried. Various liquids of known

refractive index are substituted until one is obtained which shows the outline least distinctly.

A number of liquids have been selected by various investigators to form a series in which the refractive index changes by small steps. Single compounds are preferred over mixtures, and synthetic products are better than natural oils. The following series of suitable liquids is listed in a paper by R. C. Emmons in *American Mineralogist*, 14, 482 (1929).

Since most of the compounds are relatively stable, checking with a refractometer is needed only occasionally.

<i>Liquid</i>	<i>N<sub>D</sub> 24°C.</i>
Trimethylene Chloride	1.446
Cineole	1.456
Hexahydrophenol	1.466
Decahydronaphthalene	1.477
Isoamylphthalate	1.486
Tetrachloroethane	1.492
Pentachloroethane	1.501
Trimethylene Bromide	1.513
Chlorobenzene	1.523
Ethylene Bromide + Chlorobenzene	1.533
o-Nitrotoluene	1.544
Xylidine	1.557
o-Toluidine	1.570
Aniline	1.584
Bromoform	1.595
Iodobenzene + Bromobenzene	1.603
Iodobenzene + Bromobenzene	1.613
Quinoline	1.622
$\alpha$ -Chloronaphthalene	1.633
$\alpha$ -Bromonaphthalene + $\alpha$ -Chloronaphthalene	1.640
$\alpha$ -Bromonaphthalene + $\alpha$ -Chloronaphthalene	1.650
$\alpha$ -Bromonaphthalene + $\alpha$ -Iodonaphthalene	1.660
$\alpha$ -Bromonaphthalene + $\alpha$ -Iodonaphthalene	1.670
$\alpha$ -Bromonaphthalene + $\alpha$ -Iodonaphthalene	1.680
$\alpha$ -Bromonaphthalene + $\alpha$ -Iodonaphthalene	1.690
Methylene Iodide + Iodobenzene	1.700
Methylene Iodide + Iodobenzene	1.710
Methylene Iodide + Iodobenzene	1.720
Methylene Iodide + Iodobenzene	1.730
Methylene Iodide	1.738

## Eastman Organic Chemicals as Analytical Reagents

### XXIV Reagents for Molybdenum.

#### ETHYL ETHER

Blair, *CHEMICAL ANALYSIS OF IRON*  
7th Ed., p. 210

The steel sample is dissolved with nitric acid and evaporated to dryness. After taking up in hydrochloric acid (specific gravity 1.1) it is cooled and shaken twice with ether, which extracts all of the molybdenum together with part of the iron. Chromium, nickel, manganese, and copper remain in the acid solution. The iron and molybdenum in the ether are separated later by shaking with water and precipitating the molybdenum with hydrogen sulfide.

#### PHENYLHYDRAZINE

Spiegel and Maas, *BER.* 36, 512 (1903)

A solution containing one part of phenylhydrazine in four parts of 50% acetic acid gives an intense red color on heating with dilute molybdate solutions. The colored compound may be extracted with ethyl acetate or chloroform, thus increasing the sensitivity. A large excess of phenylhydrazine is required. Tungstates, vanadates, arsenates, antimonates, or chromates do not give this reaction, nor do salts of tin, iron, or manganese.

#### POTASSIUM ETHYL XANTHATE CHLOROFORM

D. Hall, *J. A. C. S.* 44, 1462 (1922)

The separation of molybdenum occurring as an impurity in tungsten is made by forming molybdenum xanthate, which may be extracted with an organic solvent. The acid solution, which should contain about 5 mg. of Mo, is neutralized and solid potassium ethyl xanthate added. The solution is carefully re-acidified with a few drops of sulfuric acid and extracted with chloroform. After

shaking the red chloroform layer with water to remove soluble salts, it is evaporated to dryness. The residue is taken up with nitric acid and the molybdenum, which is now free of tungsten, is determined by any of the standard methods.

#### TANNIC ACID

G. Spurge, *CHEM. ENG. MINING REV.* 11, 258 (1919)

Molybdenum in ores containing less than 2% of the metal can be determined by its color reaction with tannic acid. In acetic acid solution, tannic acid forms colors with molybdates, which are red, brown, or lemon-yellow, depending on the amount of molybdenum present. These colors are then matched against suitable standards.

## Twenty New Eastman Organic Chemicals

The chemicals that are announced below have been added to our stock since the publication of List No. 23, in January. Purity specifications and prices of these new compounds will be furnished on request.

#### Acridone

o-Aminodiphenyl

p-Aminodiphenyl

iso-Butyramide

Ethyl Furoylacetate

p-Fluoroiodobenzene

m-Hydroxydiphenyl

m-Iodobenzoic Acid

1-Methyl-2-pyridone

$\beta$ -Phenoxy- $\beta'$ -chloroethyl Ether

Phenyl n-Butyl Ketone

Phenylmercuric Nitrate

Phenylpropionitrile

iso-Phthalic Acid

Propylenediamine

Pyromellitic Acid

Sodium m-Diphenylbenzenesulfonate

Sodium p-Diphenylbenzenesulfonate

Tetrahydrofurfuryl Salicylate

2,4,2',4'-Tetranitrodiphenyl